

# BRITISH MEDICAL JOURNAL

LONDON SATURDAY 1 JANUARY 1966

## Pointers

**Hastings Centenary Meeting :** 21-24 April (see p. 6).

**Vaccination Against Leprosy :** Dr. J. A. Kinnear Brown and Miss M. M. Stone find that B.C.G. vaccination conferred on children substantial protection against early forms of leprosy (p. 7). Leader on this page.

**Hypertension and Cerebral Infarction :** Dr. John Prineas and Dr. John Marshall show that patients with cerebral infarction can be separated into two distinct groups, based on the diastolic blood-pressure (p. 14).

**Arterial Occlusion in Lower Leg :** High incidence found by Mr. J. Kennedy Watt in patients with intermittent claudication (p. 18).

**Techniques of Haemoglobin Estimation :** Investigation of seven different methods by Dr. P. C. Elwood and Dr. A. Jacobs (p. 20). Leader at p. 4.

**Iatrogenic Urinary-tract Infections :** Using special methods, Mr. E. B. Gonzalez reduced the incidence of post-prostatectomy infection (p. 24). Mr. P. McR. Higgins concludes that infection from careful instrumentation is uncommon, and that its incidence is not reduced by antibiotics (p. 26).

**Phrynoderma :** Dr. A. B. Shrank's results "exclude conclusively both a deficiency of vitamin A and of essential fatty acids as the cause" (p. 29).

**Amyloidosis Presenting as Urticaria :** Case report (p. 31).

**Central Retinal Artery Occlusion :** Report of a successfully treated case by Dr. M. A. Nanjiani (p. 32).

**Prevention of Tetanus :** Recommendations by Professors D. R. Laurence and D. G. Evans, F.R.S., and Dr. J. W. G. Smith (p. 33). Letter at p. 47.

**Intensive Therapy Unit :** Described by Dr. Ronald Finn and his colleagues (p. 39).

**Mentally Handicapped Children :** Dr. B. H. Kirman describes an advisory service (p. 41).

**Medical Education Overseas :** Report of a conference (p. 44).

**Pertinax :** "Without Prejudice" (p. 45).

**New Rubella Syndrome :** Letter from Dr. J. A. Dudgeon (p. 46).

**Diagnosis of Hysteria :** Letters at p. 48.

**Woodworm and Dysentery :** Isolation of *Shigella sonnei* from worm hole in lavatory seat reported by Dr. Mair Thomas (p. 52).

**Examination Rooms :** Valuable in general practice, says Dr. R. A. Murray Scott (p. 52).

**Some B.M.A. Events in 1965 :** Summary (Supplement, p. 1).

**G.M.S. Committee :** Report (Supplement, p. 3).

## Vaccination against Leprosy

No specific vaccine is available for protection against leprosy, because the causative organism, *Mycobacterium leprae*, has not been cultured *in vitro*. J. M. M. Fernandez in 1939<sup>1</sup> suggested that B.C.G. vaccination might confer some protection because of the possible existence of a common antigen in B.C.G. and *M. leprae*. There followed several small trials of B.C.G. vaccination against leprosy, and although there was some suggestion of protection none was on a large enough scale or well enough controlled to withstand critical analysis. The present uncertainty about the value of B.C.G. vaccination against leprosy recalls the doubts about the value of B.C.G. against tuberculosis before the trials undertaken by the Medical Research Council in Britain in 1956.<sup>2</sup> Therefore the first progress report on a large-scale trial of B.C.G. vaccination of children against leprosy, which appears at page 7 of the *B.M.J.* this week, is a most important contribution to a difficult and controversial subject.

Dr. J. A. Kinnear Brown and Miss M. M. Stone describe an investigation into the prophylactic effect of B.C.G. vaccine planned by the Uganda Government with continuing scientific and technical guidance by the Leprosy Committee of the Medical Research Council. The controlled trial was initiated in September 1960 in the Teso District of Eastern Uganda, and by September 1962 19,079 children, more than 80% of whom were aged under 10 years, had been included. All were relatives or contacts of patients known to have leprosy. All the children were examined and were tuberculin-tested by the Heaf multiple puncture method. The children with negative reactions (grade 0) or with weak positive reactions (grade I or II) were assigned at random either to an unvaccinated group (8,152 children) or to a B.C.G. (freeze-dried) vaccinated group (8,149 children). Those with positive grade III or grade IV reactions (1,096) were all left unvaccinated, as were children (390) who already had skin lesions due to leprosy. The efficiency of the first follow-up between May 1963 and May 1964 was remarkable. By one means or another the investigators re-examined 94% of the children within one to three years of entry to the trial. The present report is of a preliminary nature, and the periodic examinations are continuing.

The main basis of the comparison in the report is the incidence of new cases of leprosy detected in the unvaccinated and vaccinated groups (16,301 children) within the first three years of entry into the trial. The most stringent precautions were taken to avoid any bias at the time of the follow-up examination. In particular no records of B.C.G. vaccination were available to the examiners, and a piece of adhesive paper was placed on every child on the site where vaccination would have been made, whether they were vaccinated or unvaccinated, in order to conceal the presence of a vaccination scar from the examiner. In the vaccinated and unvaccinated groups there were 107 cases of leprosy, 89 among the 8,071 unvaccinated children and 18 among the 8,091 B.C.G. vaccinated children. Thus the incidence in the unvaccinated children was 11.0

per thousand and in the vaccinated children 2.2 per thousand. The probability of this difference arising by chance is less than one in a million. Thus under the conditions of this trial B.C.G. vaccination reduced the incidence of leprosy by 80%.

This work shows beyond doubt the benefit of B.C.G. vaccine in preventing the development of leprosy in young children with negative or weak tuberculin reactions who are at special risk by being exposed to relatives or contacts with leprosy of lepromatous or tuberculoid type. The most surprising finding was that B.C.G. vaccination gave much the same protection (80%) against leprosy as was obtained by the Medical Research Council in their trials against tuberculosis.<sup>2</sup> However, these results are consistent with the recent observations that B.C.G. vaccination diminishes the multiplication of *M. leprae* in experimental leprosy in the mouse foot-pad.<sup>3</sup> Very wisely, Kinnear Brown and Stone are cautious in suggesting that their preliminary results will be as significant after a longer follow-up. The reason for their caution is that leprosy is a slowly developing chronic disease of variable course, and spontaneous healing occurs in some children with early tuberculoid-type lesions. This latter point is emphasized because all the cases of leprosy found so far in the follow-up period were of the early tuberculoid type. Furthermore, follow-up at one to three years of the children with leprosy detected at intake showed that in 8% the disease had resolved completely and in a further 21% it appeared to be resolving at the time. Only continuing regular follow-up will determine whether B.C.G. vaccination protects against fully developed tuberculoid leprosy, which if left untreated may lead to severe nerve damage. In Uganda, as in most of Africa, some 90% of leprosy is of the tuberculoid type. The more severe and highly infectious lepromatous type affects some 8% of patients in the Teso area, and in the first follow-up period no lepromatous cases were found in these children. Again, it is hoped that the trial will be continued in order to see whether B.C.G. vaccination protects also against leprosy of lepromatous type. In this respect the large-scale trial of this vaccine started recently by the World Health Organization<sup>4</sup> in Burma will be of particular importance, because there the proportion of lepromatous disease is between 40 and 70%.

Although it will be essential to continue the follow-up in this Uganda trial for at least a further five years, the prophylactic effect of B.C.G. already seen against the development of early cases of tuberculoid leprosy in children suggests that this measure should be incorporated now into programmes of leprosy control. Because the peak incidence of the disease is reached at the age of 15 years there is a good case for vaccinating within the first year of life and certainly all children up to the age of 15 years. The recent recommendation by the W.H.O. Expert Committee on Tuberculosis<sup>5</sup> that B.C.G. vaccination can be safely given without prior tuberculin testing indicates that it could be incorporated into schemes for the control of leprosy without employing specially trained staff. Finally, the results of the Uganda B.C.G. trial come soon after publication of some preliminary results from a continuing, long-term study in India,<sup>6</sup> which shows that dapsone may have a prophylactic effect in persons exposed to leprosy. The two together may

thus provide for the first time preventive measures which will help to eradicate once and for all this dreaded infection.

## Hypertrophic Obstructive Cardiomyopathy

In 1957 Sir Russell (now Lord) Brock described "Functional obstruction of the left ventricle,"<sup>1</sup> and D. Teare the following year described the morbid anatomy under the title "Asymmetrical hypertrophy of the heart."<sup>2</sup> The condition has now become known in Great Britain as hypertrophic obstructive cardiomyopathy<sup>3,4</sup> and in the United States as idiopathic hypertrophic subaortic stenosis.<sup>5</sup> A recent Ciba Foundation Symposium<sup>6</sup> and American Heart Association Monograph<sup>7</sup> show how surprisingly frequent this disorder is now that precise haemodynamic study and angiocardiology have stripped it of many of its disguises.

The main feature of it is a grotesquely hypertrophied cardiac muscle which contracts with unusual force but whose growth is unexplained by structural abnormality or hypertension. In this it differs from all other primary disorders of heart muscle. Obstruction to ventricular ejection seemingly results from over-exuberant myocardial activity, and impediment to ventricular filling follows from the relative indistensibility of the massively thickened ventricular walls. There results the great cardiac mimic, typically resembling organic aortic stenosis or mitral incompetence or both, but able to simulate mitral or tricuspid stenosis, ventricular or atrial septal defect, and, least often, other forms of cardiomyopathy.

The aetiology is unknown; a familial incidence is noted in about one-third of cases. The sexes are probably affected equally, but E. Braunwald and colleagues<sup>7</sup> found the familial form to be commoner in males. The condition has been described in the newborn baby,<sup>8</sup> is seen in childhood, but most often presents in the third decade. Though usually progressive, arrest or even regression of the obstruction sometimes occurs.

Afflicted persons are often of athletic disposition and good physical development. Heart failure and atrial fibrillation are rare. The haemodynamic abnormality determines some characteristic physical signs. The left ventricle starts to empty abnormally fast but obstructs itself before completion of ejection by apposition of its hypertrophied walls. Dizzy spells, syncope, angina, and sudden death are distressingly frequent, though in contrast to organic aortic stenosis the arterial pulses are full and jerky. A murmur which is maximal at the lower left sternal edge but only poorly conducted to the base of the heart and carotid arteries is heard late in systole and coincides with the delayed onset of obstruction. Neither ejection clicks nor early diastolic murmurs are heard and calcium is not found in the aortic valve. Functional mitral incompetence also begins when the outflow becomes obstructed, and may contribute to the late systolic murmur, which then sometimes radiates to the axilla. Since the thick left ventricle requires an abnormally high venous filling pressure, the patient suffers severe dyspnoea, and the physician detects a forceful presystolic atrial beat giving a double impulse which seems excessive for the apparent severity of the "aortic stenosis."

In some cases obstruction in the left ventricle during systole is absent and obstruction during diastole dominates

<sup>1</sup> Fernandez, J. M. M., *Rev. argent. Dermatosis*, 1939, 23, 425.

<sup>2</sup> Medical Research Council, *Brit. med. J.*, 1956, 1, 413.

<sup>3</sup> Shepard, C. C., *Amer. J. Epidem.*, 1965, 81, 150.

<sup>4</sup> World Health Organization. Report MHO/PA/131.64. 1964. Geneva.

<sup>5</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1964, 290.

<sup>6</sup> *J. Amer. med. Ass.*, 1965, 192, Med. News p. 34.